REMARKS

The Office Action dated March 23, 2004, has been received and reviewed. Claims 1-51 are pending in the present application. Claims 1-16 stand rejected. Claims 17-51 have been withdrawn and Applicants have cancelled these claims without prejudice or disclaimer. Claims 52-59 have been added. Applicants respectfully request reconsideration of the application in view of the arguments below.

I. Claim Amendments

Applicants have amended independent claims 1, 9 and 16 to include the proviso that the pharmaceutically acceptable carrier is not a buccal dosage unit. Applicants have added claims 52-59 which mirror claims 1-8 except for the proviso that the pharmaceutically acceptable carrier is not a bioerodible polymeric carrier. Applicants have cancelled claims 17-51 without prejudice or disclaimer in view of the restriction requirement.

II. Rejections under 35 U.S.C. § 103(a)

Claims 1-16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Place, U.S. Patent No. 6,284,263, (hereinafter "Place"), in view of Estok, U.S. Patent No. 6,011,043, (hereinafter "Estok"). Applicants traverse this rejection for the reasons set forth below.

To establish a prima facie case of obviousness, the prior art reference or references when combined must teach or suggest *all* the recitations of the claim, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). To support combining references, evidence of a suggestion, teaching, or motivation to combine must be clear and particular, and this requirement for clear and particular evidence is not met by broad and conclusory statements about the teachings of

references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Furthermore, as recently affirmed by the Court of Appeals for the Federal Circuit in *In re Sang-su Lee*, a factual question of motivation is material to patentability, **and cannot be resolved on subjective belief and unknown authority**. *See In re Sang-su Lee*, 277 F.3d 1338 (Fed. Cir. 2002). Respectfully, as will be discussed below, the Official Action fails to meet the requirements for a prima facie showing of obviousness under § 103.

Applicants submit that Place, either alone or in combination with Estok, fails to teach or suggest the elements of claims 1-16 of the present application. Claims 1 and 16 of the present application recite a composition for the treatment of a sexual dysfunction comprising a therapeutically effective amount of an estrogenic compound; a therapeutically effective amount of an androgenic compound; a therapeutically effective amount of a vasodilation compound; and a pharmaceutically acceptable carrier. Claim 9 recites a composition for the treatment of a sexual dysfunction comprising a therapeutically effective amount of an androgenic compound, a therapeutically effective amount of a vasodilation compound, and a pharmaceutically acceptable carrier. All now contain the recitation "with the proviso that the pharmaceutically acceptable carrier is not a buccal dosage unit".

Place includes a combination of an estrogen, an androgenic compound and a progestin for use in a buccal drug delivery. Place teaches away from any other type of delivery as "[w]ith oral administration, as is true with the oral administration of many steroid hormones, estrogens tend to be inactivated." Col. 2, lines 3-5. Place further notes that this first pass effect may lead to undesirable undesirable increase in the production of certain coagulation factors and other biologically important compounds by the liver. Col. 2, lines 8-10. Furthermore, Place teaches "avoids both gastrointestinal degradation of the drug and the "first pass" effect in the liver encountered with oral formulations, and enables the use of smaller doses of active agents (and thus avoids the side effects associated with conventional formulations)".

Col. 2, lines 31-35. Thus, Place teaches away from the present invention as no combination of Place with Estok teaches or suggests the elements of the claims of the present application.

Furthermore, the composition taught by Place includes a progestin. Applicants note that a progestin often leads to a scheduled withdrawal bleed or period in a high percentage of women undergoing hormone replacement therapy. Therefore, Place merely notes a composition that leads to a scheduled withdrawal bleed or period in a high percentage of women which teaches away from the composition recited in independent claims 1, 9 and 16 of the present application along with their dependent claims. Additionally, Place fails to teach or suggest a composition further comprising a vasodilation compound as recited in claim 1, 9 and 16 of the present application. In summation, one of skill in the art would be led not to try anything but a buccal dose unit if they followed the teachings of Place. Accordingly, Applicants submit that Place either alone or in combination with the other cited references fails to teach or suggest the recitations of claims 1-16.

Applicants further submit that Estok, either alone or in combination with Place, fails to teach or suggest all of the elements of Claims 1-16 of the present application. Estok notes that phentolamine may be used in a method of treating sexual dysfunction. Furthermore Estok combines phentolamine with an opitate, namely morphine, with zinc chloride to produce apomorphine. Estok provides no basis for any estrogens or androgens to be used in a pharmaceutical composition as recited in independent claims 1, 9 and 16 of the present invention. Furthermore, Estok states that female sexual dysfunction may include orgasmic dysfunction due to clitoral irregularities or disturbances, as well as arousal disorder, which is the inability to engorge and/or lubricate the vaginal wall. *See,* Cols. 1-2, lines 66-67 and 1-3. The present application states that sexual dysfunction is "related to such aspects of female sexuality including overall physiological health of the vagina, integrity of the vaginal epithelium, and the ability of the vagina to produce sufficient lubrication." Applicants further submit the overall health benefits are not disclosed or understood by Estok.

The Office Action states that it would be obvious to combine the cited references in order to make the claimed invention because "it is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a

third composition that is to be used for the very same purpose." Applicants submit that these references fail to contain any motivation to combine their teachings as required by *In re Sang-su Lee* and in fact Place teaches away from the present invention. Applicants further submit the overall health benefits of the composition of the present application are not suggested or taught by Place and Estok. Applicants further submit that one of skill in the art would have not combined the two references due to these benefits. Accordingly, Applicants submit that there is no motivation to combine the teachings of Place and Estok to recite the elements of independent claims 1, 9 and 16 of the present invention of which claims 2-8 and 10-15 depend from respectively. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejections to claims 1-16.

ENTRY OF AMENDMENTS

The amendments to the claims above should be entered by the Examiner because the amendments are supported by the as-filed specification and drawings and do not add any new matter to the application. Further, Applicant believes that the amendments do not raise new issues or require a further search. Applicant further submits pursuant to 37 C.F.R. § 1.116, amendments after final presenting rejected claims in better condition for allowance may be admitted.

CONCLUSION

In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

It is not believed that an extension of time and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,

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